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Proposed Registration Document PRD2014-11

Hydrogen Peroxide

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Overview

Proposed Registration Decision for Hydrogen Peroxide

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing full registration for the sale and use of Interox M-70 Hydrogen Peroxide, Interox CPMC-50 and Interox Paramove 50, containing the technical grade active ingredient hydrogen peroxide, for the treatment of sea lice on Atlantic salmon reared in marine aquaculture sites.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

This Overview describes the key points of the evaluation, while the Science Evaluation provides detailed technical information on the human health, environmental and value assessments of Interox M-70 Hydrogen Peroxide, the manufacturing concentrate Interox CPMC-50 and the end-use product Interox Paramove 50.

What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable[1] if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its proposed conditions of registration. The Act also requires that products have value[2] when used according to the label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (for example, children) as well as organisms in the environment (for example, those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the Pesticides and Pest Management portion of Health Canada's website at healthcanada.gc.ca/pmra.

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1 "Acceptable risks" as defined by subsection 2(2) of the *Pest Control Products Act*.

2 "Value" as defined by subsection 2(1) of the *Pest Control Products Act*: "the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (*a*) efficacy; (*b*) effect on host organisms in connection with which it is intended to be used; and (*c*) health, safety and environmental benefits and social and economic impact."

Before making a final registration decision on hydrogen peroxide, the PMRA will consider all comments received from the public in response to this consultation document.[3] The PMRA will then publish a Registration Decision[4] on hydrogen peroxide, which will include the decision, the reasons for it, a summary of comments received on the proposed final registration decision and the PMRA's response to these comments.

For more details on the information presented in this Overview, please refer to the Science Evaluation of this consultation document.

What Is Hydrogen Peroxide?

Hydrogen peroxide (H_2O_2) is the active ingredient in Interox Paramove 50. Hydrogen peroxide is a strong oxidizer which is widely used in aquaculture for sea lice control. While the exact mode of action of hydrogen peroxide is not known, H_2O_2 temporarily paralyzes sea lice, causing them to fall off of the salmon host. H_2O_2 also reduces egg string viability. In addition, attached sea lice life stages have a reduced ability to re-attach to the host after treatment with H_2O_2.

Health Considerations

Can Approved Uses of Hydrogen Peroxide Affect Human Health?

Hydrogen peroxide is unlikely to affect human health when it is used according to label directions.

Exposure to hydrogen peroxide may occur when handling the end-use product, Interox Paramove 50, which has a commercial use to treat sea lice in farmed salmon. When assessing health risks, two key factors are considered: the levels where no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

The technical grade active ingredient, hydrogen peroxide, is considered to be highly acutely toxic by the oral route, slightly acutely toxic by the dermal route, and moderately acutely toxic by the inhalation route. It is corrosive to both skin and eyes, and is not a dermal sensitizer. Signal words and cautionary statements alerting users to the potential for acute toxicity, as well as corrosivity to skin and eyes, are required on the technical grade active ingredient, manufacturing use product, and end-use product labels.

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3 "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

4 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

Residues in Water and Food

Dietary risks from food and water are not of concern.

Food residue exposure from use of Interox Paramove 50 is not expected to appreciably increase levels of hydrogen peroxide over endogenous levels in treated fish due to the rapid decomposition of hydrogen peroxide to water and oxygen upon contact with moisture and degradation in blood and tissues. The PMRA has also determined that a maximum residue limit (MRL) is not required for Interox Paramove 50.

Occupational Risks From Handling Interox Paramove 50

Occupational risks are not of concern when Interox Paramove 50 is used according to the proposed label directions, which include protective measures.

Interox Paramove 50 is applied to farmed Atlantic salmon using wellboats or by enclosing the farm sea cages with tarpaulins. Depending on which method of application is used, workers involved in handling, storing, transferring, mixing, loading, applying the product, and in clean-ups/repair and activities immediately after application, could come into contact with residues of the product on the skin or in the eyes or inhale hydrogen peroxide vapours. Therefore, the label specifies that anyone involved in these activities must wear chemical resistant coveralls, a long-sleeved shirt and pants, a chemical splash proof face shield, socks, and chemical-resistant boots and gloves. Workers involved in application and post-application activities for Interox Paramove 50 using the tarpaulin method must also wear a NIOSH approved respirator for hydrogen peroxide. This personal protective equipment (PPE) along with the other precautionary and hygiene statements on the label is considered adequate to protect workers from any unnecessary risks due to occupational exposures.

Bystanders can only enter fish farms with permission of the owners and precautionary statements on the label prevent recreational activities in the water around the fish farms until the treatments are complete and tidal flushing occurs. Therefore, health risks to bystanders are not of concern.

Environmental Considerations

What Happens When Hydrogen Peroxide Is Introduced Into the Environment?

Hydrogen peroxide enters the environment when applied to treat sea lice on farmed salmon. The product can be applied directly into net pens in open water or into wellboats containing salmon. Hydrogen peroxide is highly reactive in natural waters and breaks down rapidly to form water and oxygen. It is not expected to accumulate over time in either sediment or in the water column. Hydrogen peroxide dissolves easily in water and is unlikely to move into sediments. Hydrogen peroxide is not expected to enter the atmosphere or be subject to long-range transport. Hydrogen peroxide does not readily bind to organic matter and is not expected to accumulate in animals or plants.

When used according to label directions, the end-use product, Interox Paramove 50 is expected to pose a negligible risk to mammals, crustaceans, amphibians, birds, or fish. The use of Interox Paramove 50 may pose a short term risk to marine algae located close to the treated aquaculture net pens and wellboat flushing pipes. Due to the rapid reproduction rates of algae species coupled with the introduction of new algae populations by tidal flushing, hydrogen peroxide is not expected to pose a risk to algae populations. Label statements are required on the product labels to inform the users of the potential risks.

Value Considerations

What Is the Value of Interox Paramove 50?

Hydrogen peroxide is used to treat farmed Atlantic salmon infested with sea lice.

Interox Paramove 50 has value as a bath treatment for use against sea lice as it is effective at removing pre-adult and adult life stages from infested Atlantic salmon. Sea lice are a highly detrimental pest to farmed Atlantic salmon; heavy infestations can result in effects ranging from high mortality up to complete loss of infested fish. While some dislodged sea lice may re-attach to fish following treatment, the risk of re-infestation can be mitigated using various methods to physically capture the dislodged sea lice.

Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law.

The key risk-reduction measures being proposed on the label of Interox Paramove 50 to address the potential risks identified in this assessment are as follows.

Key Risk-Reduction Measures

Human Health

The signal words 'DANGER – POISON, CORROSIVE TO EYES AND SKIN' are required on the principal display panel of the technical grade active ingredient, the manufacturing use product, and end-use product labels. The statements 'Fatal or poisonous if swallowed', 'May be harmful if absorbed through the skin', 'May be fatal if inhaled', 'Corrosive to the eye and skin', and 'Do not get in eyes or on skin' are required on the secondary display panel of both the technical grade active ingredient and end-use product labels.

Because there is a concern with users coming into direct contact with Interox Paramove 50 on the skin, in the eyes or through the inhalation of vapours of hydrogen peroxide, the statement, "when using wellboats, all workers/personnel involved in handling, storing, transferring, mixing, loading, applying the concentrate, clean-ups/repair and in activities immediately after

application, must wear chemical resistant coveralls (Tyvek or PVC full chemical splash protective suit) over a long-sleeved shirt and long pants, chemical splash proof face shield, socks, and chemical-resistant boots and gloves." must appear in the PRECAUTIONS section of the secondary display panel of the label for the end-use product to mitigate any potential occupational exposures.

Similarly, for sea cage (tarpaulin) applications, the statements, "when applying to sea cages, all workers/personnel involved in handling, storing, transferring, mixing, loading, applying the concentrate, clean-ups/repair and in activities immediately after application, must wear a NIOSH-approved respirator for hydrogen peroxide (www.cdc.gov/niosh/npg/npgdo0335.html), chemical resistant coveralls (Tyvek or PVC full chemical splash protective suit) over a long-sleeved shirt and long pants, chemical splash proof face shield, socks, and chemical-resistant boots and gloves. Observe respirator use limitations specified by NIOSH and the manufacturer." must appear in the PRECAUTIONS section of the secondary display panel of the label for the end-use product.

Finally, to prevent bystander (for example, recreational boaters and fishers) exposures to hydrogen peroxide, the following statements are required in the PRECAUTIONS section of the secondary display panel of the label for the end-use product: "It is recommended entry to fish farm areas is restricted until all treatments are completed. It is also recommended that recreational activities in treated water near fish farm areas are not permitted until tidal flushing occurs."

Environment

- A label statement is required indicating toxicity to aquatic organisms.
- Treatments are limited to net pens enclosed by a skirt or a tarpaulin and treatments carried out in the well of a wellboat.
- The product is classified as restricted and a use permit must be obtained from the province prior to any treatment.

Next Steps

Before making a final registration decision on hydrogen peroxide, the PMRA will consider all comments received from the public in response to this consultation document. The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. Please forward all comments to Publications (contact information on the cover page of this document). The PMRA will then publish a Registration Decision, which will include its decision, the reasons for it, a summary of comments received on the proposed final decision and the Agency's response to these comments.

Other Information

When the PMRA makes its registration decision, it will publish a Registration Decision on hydrogen peroxide (based on the Science Evaluation of this consultation document). In addition, the test data referenced in this consultation document will be available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa).

Science Evaluation

Hydrogen Peroxide

1.0 The Active Ingredient, Its Properties and Uses

1.1 Identity of the Active Ingredient

Active substance	Hydrogen peroxide
Function	Acaricide
Chemical name	
1. **International Union of Pure and Applied Chemistry (IUPAC)**	Hydrogen peroxide
2. **Chemical Abstracts Service (CAS)**	Hydrogen peroxide
CAS number	7722-84-1
Molecular formula	H_2O_2
Molecular weight	34.014
Structural formula	HO—OH
Purity of the active ingredient	70.0%

1.2 Physical and Chemical Properties of the Active Ingredient, Manufacturing Concentrate and End-use Product

Technical Product—Interox M-70 Hydrogen Peroxide

Property	Result
Colour and physical state	Colourless liquid
Odour	Odourless
Melting range	N/A
Boiling point or range	125°C (hydrogen peroxide decomposes)
Density	1.278-1.299 g/cm^3 at 20°C
Vapour pressure at 30°C	200 Pa
Ultraviolet (UV)-visible spectrum	No significant absorbance expected at $\lambda > 300$ nm
Solubility in water	Product is an aqueous solution and will be completely miscible with water

Property	Result
Solubility in organic solvents	Product is an aqueous solution and will be miscible with many polar organic solvents
n-Octanol-water partition coefficient (K_{ow})	Log K_{ow} = -1.57 (calculated)
Dissociation constant (pK_a)	11.62
Stability (temperature, metal)	Hydrogen peroxide is unstable when exposed to heat, sunlight or metals/metal salts

Manufacturing Concentrate—Interox CPMC-50

Property	Result
Colour	Colourless
Odour	Pungent
Physical state	Liquid
Formulation type	Solution (SN)
Guarantee	50.0%
Container material and description	Metal, plastic, ISO containers and IBCs (intermediate bulk containers) (100 L – bulk)
Density	1.192-1.200 g/cm^3 at 20°C
pH	< 3
Oxidizing or reducing action	Product is an oxidizing solution
Storage stability	Hydrogen peroxide is stable when stabilizers are added and stored under ambient conditions. Hydrogen peroxide will decompose when exposed to heat.
Corrosion characteristics	Product is not expected to be corrosive to the packing material
Explodability	Product is not explosive

End-use Product—Interox Paramove 50

Property	Result
Colour	Colourless
Odour	Pungent
Physical state	Liquid
Formulation type	Solution (SN)
Guarantee	50.0%
Container material and description	Metal, plastic, ISO containers and IBCs (intermediate bulk containers) (100 L – bulk)
Density	1.192-1.200 g/cm^3 at 20°C
pH of 1% dispersion in water	< 3
Oxidizing or reducing action	Product is an oxidizing solution
Storage stability	Hydrogen peroxide is stable when stabilizers are added and stored under ambient conditions. Hydrogen peroxide will decompose when exposed to heat.

Property	Result
Corrosion characteristics	Product is not expected to be corrosive to the packing material
Explodability	Product is not explosive

1.3 Directions for Use

Interox Paramove 50 is administered as an external bath treatment by either using wellboats or completely enclosed tarpaulins. Treat only when thresholds are reached. Allow for a minimum of 7 days between applications. Do not apply more than 5 applications of Interox Paramove 50 per year. The optimum treatment to remove infestations of sea lice is an immersion in a solution of Interox Paramove 50 at a concentration of 1500 ppm of hydrogen peroxide for a period of 20 minutes at temperatures up to 13°C (55°F). Interox Paramove 50 treatments may be extended for up to 30 minutes if desired. Shorten treatment time if water temperature is higher than 13°C. Temperatures greater than 13°C and/or exposures longer than 20 minutes may result in damage or mortality of treated fish. Use extreme caution when applying at higher temperatures. Discontinue treatment and flush with sea water immediately if signs of distress in fish are observed. Efficacy of treatment may be reduced when using concentrations below 1500 ppm. The fish to be treated must either be crowded into a small area of the production net and completely encircle with a tarpaulin or transferred into a wellboat confinement area.

2.0 Methods of Analysis

2.1 Methods for Analysis of the Active Ingredient

The methods provided for the analysis of the active ingredient and the impurities in Interox M-70 Hydrogen Peroxide have been assessed to be acceptable for the determinations.

2.2 Method for Formulation Analysis

The method provided for the analysis of the active ingredient in the formulations has been assessed to be acceptable for use as an enforcement analytical method.

3.0 Impact on Human and Animal Health

3.1 Toxicology Summary

A detailed review of the toxicological database for the active ingredient hydrogen peroxide consisting of waiver rationales and published data was conducted. The scientific quality of the data is acceptable and the database is sufficiently complete to define the majority of the toxic effects that may result from exposure resulting from the intended use of this pest control product.

A data waiver rationale was submitted for all toxicity data, citing that the toxicity of hydrogen peroxide has been well-characterized in the published scientific literature. The acute toxicity of hydrogen peroxide has been well characterized in publicly available scientific literature. The main mode of action is based on its strong oxidizing and corrosive properties, with its oral,

dermal and inhalation toxicities being secondary to corrosivity. It is considered to be highly acutely toxic by the oral route, slightly acutely toxic by the dermal route, and moderately acutely toxic by the inhalation route. It is corrosive to both skin and eyes, and is not a dermal sensitizer.

Due to the rapid degradation of hydrogen peroxide, the hazard posed by the proposed end-use product is mostly of an acute nature. However, several short-term toxicity studies have been conducted with hydrogen peroxide, with the test substance administered in the diet or drinking water. The main effect observed from hydrogen peroxide administration over three to ten weeks was decrease in body weight gain and reduced water consumption, likely due to the odour and irritant properties of the compound. Stability of hydrogen peroxide in drinking water and feed during the tests was of concern and consequently the results were viewed with caution in the hazard assessment.

Developmental toxicity information for hydrogen peroxide was not available at the time of evaluation. However, based on the toxicological information that was available, coupled with a long history of human exposure as a commodity chemical around the world and its use as a pesticide in the United States, it appears unlikely that treatment related effects will result from maternal exposure to hydrogen peroxide.

Hydrogen peroxide has been shown to be mutagenic in vitro, but is not genotoxic in vivo due to its rapid decomposition to water and oxygen. Since hydroxyl radicals and singlet oxygen are capable of damaging DNA directly, the genotoxic potential of hydrogen peroxide depends on the accessibility of the hydroxyl radical to target DNA.

Hydrogen peroxide was tested for carcinogenicity in mice by oral and dermal application and in hamsters by topical application to oral mucosa. In mice, duodenal tumours were found from oral administration, while one study in mice and one in hamsters showed no promoting activity of hydrogen peroxide, and the other studies in mice and hamsters were considered to be inadequate for evaluation. Therefore there is limited evidence of carcinogenicity in experimental animals for the carcinogenicity of hydrogen peroxide.

3.2 Occupational and Bystander Risk Assessment

3.2.1 Use Description

Interox Paramove 50 is intended for the removal of sea lice (*Lepeophtheirus salmonis* or *Caligulus elongates)* on farmed Atlantic salmon (*Salmo salar*). The proposed application methods include the treatment of salmon in wells on a wellboat or in sea cages enclosed with tarpaulins. The proposed application rates (i.e. 2.4–3.6 g Interox Paramove 50/L sea water) are based on target concentrations of hydrogen peroxide in the wells or the tarpaulins and range from 1200 to 1400 mg/L at water temperatures greater than 14°C, to 1700 to 1800 mg/L at temperatures below 8°C.

3.2.2 Mixer, Loader, and Applicator Exposure and Risk Assessment

Potential routes of occupational exposure to hydrogen peroxide during treatment of salmon with the end-use product are dermal, ocular and inhalation. The potential for such exposures during wellboat treatments is low as the wellboat is largely a closed system with Interox Paramove 50 delivered from an on board storage tank to each well via stainless steel piping directly into the water recirculation system for the wells and the amount delivered controlled by a programmable volumetric batch controller. Workers could be exposed via splashing or vapourization of the hydrogen peroxide if they are in the vicinity of the wells when the end-use product is delivered, particularly workers who are sampling the well water for hydrogen peroxide levels at regular intervals during the delivery and mixing process. However, any such exposures would be very short-term as the mixing process takes approximately 10 minutes to complete and use of the personal protective equipment (PPE) described on the label for the end-use product (for example, chemical-resistant coveralls, long-sleeved shirt and pants, face shield, socks, and chemical resistant boots and gloves) will mitigate any dermal and ocular exposures and risks.

Potential inhalation exposures and risks for wellboat applications are also expected to be minimal because the end-use product will rapidly be diluted with water during the application/mixing process and airborne concentrations of hydrogen peroxide above the wells are expected to be well below the American Conference of Governmental Industrial Hygienists time-weighted average threshold limit value (ACGIH TWA-TLV) of 1.4 mg/m^3 for hydrogen peroxide. Many provincial occupational exposure limits for hydrogen peroxide are based on the ACGIH TWA-TLV. Also, there are precautionary statements on the label advising workers not to get the product in the eyes or on the skin, and not to inhale any vapours.

There is a greater potential for dermal, inhalation, and ocular exposures for workers applying Interox Paramove 50 by the tarpaulin method, especially for those handling and operating the pumping system and distribution hoses for delivering the product to the sea cages. However, the dermal and ocular exposures and risks are expected to be minimal when workers follow the PPE instructions on the label for the product which includes the same clothing, face shield, and footwear used for the wellboat applications. To mitigate potential inhalation exposures to hydrogen peroxide vapours during the application of the end-use product to the sea cages, the use of a NIOSH-approved respirator for hydrogen peroxide is included on the label for Interox Paramove 50 for tarpaulin applications. In addition, the label precautionary statements on avoiding eye and skin contact with the product, and avoiding inhalation of any vapours also apply to the tarpaulin method of application.

The storage tanks for the end-use product on the wellboat and on the barges used for the tarpaulin applications have breather vents to release any excess vapours of hydrogen peroxide. Although it is estimated that the concentrations of hydrogen peroxide in the headspace of these tanks could exceed the ACGIH TWA-TLV, the tanks are vented to the ambient (sea) air, workers are not expected to be exposed to vapours released from the vents, and concentrations of hydrogen peroxide in the air above the vents are expected to be less than the ACGIH TWA-TLV. Consequently, inhalation exposures and risks from hydrogen peroxide vapours released from the storage tanks are expected to be negligible.

3.2.3 Post-application Exposure and Risk

There is a very low likelihood of post-application occupational dermal, inhalation or ocular exposures to hydrogen peroxide following application of Interox Paramove 50 by the wellboat method. This is because the process of flushing the wells with fresh water will rapidly reduce the concentrations of hydrogen peroxide below treatment concentrations and the pump discharge of well water from the wellboat is expected to rapidly disperse any residual hydrogen peroxide into the sea. In addition, the label for the end-use product specifies that workers involved in post-application activities must wear the same PPE used when applying the end-use product to the wells to limit dermal and ocular exposures.

For tarpaulin applications, potential post-application dermal, inhalation, and ocular exposures could occur when the tarpaulins are removed to disperse the end-use product from the sea cages, empty storage tanks and hoses are rinsed out, and divers enter the sea cages to remove dead fish after treatment. However, these exposures will be mitigated as the label for Interox Paramove 50 specifies that workers performing post-application activities must wear the same PPE as those involved in the application of the product including a NIOSH-approved respirator. Also, divers only enter the sea cages at least an hour after treatments are finished and after tidal flushing has occurred, so exposures and risks from hydrogen peroxide will be negligible.

3.2.4 Bystander Exposure and Risk Assessment

While it is likely that there will be recreational uses of the waters in the vicinity of the fish farms treated with Interox Paramove 50, recreational boaters or fishermen would only be allowed to enter farm sites with permission from the farm owner and not when sea cages are being treated with the end-use product. Also, there are precautionary statements on the label restricting entry to the farms until treatments are completed and preventing recreational activities in the waters near the fish farms until tidal flushing occurs. As a result, bystander exposures and risks from Interox Paramove 50 are expected to be negligible.

3.3 Food Residue Exposure Assessment

3.3.1 Food and Drinking Water

Dietary exposure to hydrogen peroxide may occur through consumption of treated salmon; however it is not expected to be of concern. As a result of the rapid decomposition of hydrogen peroxide to water and oxygen upon contact with moisture, the absorption, distribution, metabolism and excretion of this compound is expected to be negligible. Use of Interox Paramove 50 for the proposed use is not expected to result in increased levels of hydrogen peroxide over endogenous levels in the edible tissues of the treated fish due to rapid decomposition in the water as well as in the tissues. Due to the degradation of hydrogen peroxide in the blood it is unlikely that the compound would be systemically distributed and therefore would not affect endogenous levels in the tissues. Furthermore, the withdrawal period of 24 hours after treatment will result in further decomposition of the active ingredient prior to harvesting of fish for consumption. Therefore, food residue exposure to the end-use is not expected to be of concern.

As the end-use is to be applied in sea cages or in wellboats in the sea, and due to the rapid decomposition of hydrogen peroxide in water, exposure to hydrogen peroxide in drinking water is not expected to be of concern. Therefore, the use of Interox Paramove 50 is not expected to result in unacceptable dietary risks when the product is used according to label directions.

3.4 Exposure from Drinking Water

3.4.1 Concentrations in Drinking Water

Based on the proposed use pattern of direct application to enclosed aquaculture net pens or wellboat wells in the open ocean, hydrogen peroxide is not anticipated to enter drinking water supplies or reservoirs.

3.4.2 Maximum Residue Limits (MRLs)

As part of the assessment process prior to the registration of a pesticide, Health Canada must determine that the consumption of the maximum amount of residues that are expected to remain on food products when a pesticide is used according to label directions will not be a concern to human health. This maximum amount of residues expected is then legally established as a maximum residue limit (MRL) under the *Pest Control Products Act* for the purposes of adulteration provision of the *Food and Drugs Act*. Health Canada sets science-based MRLs to ensure the food Canadians eat is safe.

As the proposed use of Interox Paramove 50 is not expected to appreciably increase levels of hydrogen peroxide over endogenous levels in treated fish due to decomposition in water and degradation in tissues, the PMRA has not required the establishment of an MRL for hydrogen peroxide.

3.5 Incident Reports Related to Human and Animal Health

Since 26 April 2007, registrants have been required by law to report incidents, including adverse effects to health and the environment, to the PMRA within a set time frame. Information on the reporting of incidents can be found on the Health Canada website.

Incidents were searched and reviewed for products containing the active ingredient hydrogen peroxide for use as pesticides. As of 29 May 2013, there were no incidents related to human health or worker safety involving products containing hydrogen peroxide.

4.0 Impact on the Environment

4.1 Fate and Behaviour in the Environment

Once introduced to the marine environment, hydrogen peroxide is expected to remain in the water column and disperse with the prevailing ocean currents. Binding and accumulation in sediment is not expected as hydrogen peroxide is highly soluble in water. Volatilization and long-range transport are also not expected. Hydrogen peroxide is very short lived in natural aquatic environments with reported half-lives ranging from 1 hour to 10 days. The transformation products from the degradation of hydrogen peroxide are water and oxygen. Hydrogen peroxide degrades by redox reactions catalysed by micro-organisms as well as various organic and inorganic compounds such as dissolved metals, minerals and dissolved organic matter. Oceanic dispersion, in the marine environment further speeds up the aquatic dissipation of hydrogen peroxide. When the tarped or skirted net pen treatment method is used, an aquatic field dissipation time of 1 minute was observed for a reduction in concentration of 50% (DT_{50}) and an aquatic dissipation time of 10 minutes was observed to reach a reduction in concentration of 90% (DT_{90}). Concentrations are further reduced by a factor of 100 after approximately 1 hour and a factor of one thousand after 3 hours. When the wellboat treatment method is used, an aquatic field dissipation time of less than1 minute was observed for a reduction in concentration of 50% (DT_{50}) and an aquatic dissipation time of 1 minute was observed to reach a reduction in concentration of 90% (DT_{90}). Concentrations are further reduced by a factor of 100 after approximately 30 minutes and a factor of one thousand after 50 minutes.

Once released from a net pen or wellboat the hydrogen peroxide takes on the form of a plume in the marine environment. This plume is subject to horizontal movement, diffusion and elongation in the direction of the dominant current which will carry it away from the original point of release. During these processes, the total volume of water occupied by the plume increases and as a result, the concentration of hydrogen peroxide decreases over time as it is diluted and as it transforms to water and oxygen. When a net pen is used, the tarp or skirt of a net pen is dropped and the hydrogen peroxide is released instantly, whereas when a wellboat is used the treatment well of the wellboat is flushed with fresh ocean water over a period of time (approximately 60 minutes). The concentration of hydrogen peroxide being released from the wellboat is therefore decreasing over time as the concentration within the wellboat well is flushed and diluted with fresh ocean water. Consequently, the wellboat flushing pipes influence the speed, shape and direction of the plume. Generally the plume will take on a shape of a cone and dispersion rates are increased through the additional force exerted by the flushing jets.

The aquaculture industry may treat up to two adjacent net pens with hydrogen peroxide simultaneously. When released from the net pens, the two plumes containing the hydrogen peroxide may overlap. The concentration of hydrogen peroxide resulting from the overlapping area of the two plumes would be equal to the concentration in the first plume added to the concentration of the second plume. Or in other words, if the concentration in the first plume was 0.1 mg/L hydrogen peroxide and the concentration in the second plume was also 0.1 mg/L hydrogen peroxide, then the concentration of hydrogen peroxide in the waters where both plumes are overlapping would be 0.2 mg/L hydrogen peroxide.

Environmental fate data for hydrogen peroxide and its transformation products are summarized in Appendix I, Table 2.

4.2 Environmental Risk Characterization

The environmental risk assessment integrates the environmental exposure and ecotoxicology information to estimate the potential for adverse effects on non-target species. This integration is achieved by comparing exposure concentrations with concentrations at which adverse effects occur. Estimated environmental exposure concentrations (EECs) are concentrations of pesticide in various environmental media, such as food, water, soil and air. The EECs are estimated using standard models which take into consideration the application rate(s), chemical properties and environmental fate properties, including the dissipation of the pesticide between applications. Ecotoxicology information includes acute and chronic toxicity data for various organisms or groups of organisms from both terrestrial and aquatic habitats including invertebrates, vertebrates, and plants. Toxicity endpoints used in risk assessments may be adjusted to account for potential differences in species sensitivity as well as varying protection goals (i.e. protection at the community, population, or individual level).

Initially, a screening level risk assessment is performed to identify pesticides and/or specific uses that do not pose a risk to non-target organisms, and to identify those groups of organisms for which there may be a potential risk. The screening level risk assessment uses simple methods, conservative exposure scenarios (for example, 1 hour of continual exposure at the treatment dose concentration) and sensitive toxicity endpoints. A risk quotient (RQ) is calculated by dividing the exposure estimate by an appropriate toxicity value (RQ = exposure/toxicity), and the risk quotient is then compared to the level of concern (LOC). The level of concern for all marine species is 1. If the screening level risk quotient is below the level of concern, the risk is considered negligible and no further risk characterization is necessary. If the screening level risk quotient is equal to or greater than the level of concern, then a refined risk assessment is performed to further characterize the risk. A refined assessment takes into consideration more realistic exposure scenarios (such as the effects of oceanic dispersion) and might consider different toxicity endpoints. Refinements may include further characterization of risk based on exposure modelling, monitoring data, results from field or mesocosm studies, and probabilistic risk assessment methods. Refinements to the risk assessment may continue until the risk is adequately characterized or no further refinements are possible.

4.2.1 Risks to Terrestrial Organisms

Due to the application pattern, fast degradation rates and low potential for bioaccumulation, exposure to terrestrial organisms including terrestrial invertebrates, pollinators, beneficial arthropods, birds, terrestrial mammals, terrestrial plants, earthworms and soil microorganisms to Interox M-70 Hydrogen Peroxide, Interox CPMC-50 and Interox Paramove 50 from direct application to aquaculture net pens or application in a wellboat is not anticipated.

4.2.2 Risks to Aquatic Organisms

A risk assessment for hydrogen peroxide was conducted for marine aquatic organisms based on available toxicity data. A summary of marine aquatic toxicity data for hydrogen peroxide is presented in Appendix I, Table 3. To assess the potential effects from exposure to hydrogen peroxide, the estimated environmental concentration (EEC) in the marine environment was compared to the non-target organism endpoints. An uncertainty factor of 2 was applied to all invertebrate and algae endpoints. Risk quotients were calculated using one of the following formulas: RQ = EEC / (most sensitive species (LC_{50}/2 for invertebrates and EC_{50}/2 for algae)). Given the very short field dissipation times, chronic exposure to aquatic organisms is not anticipated. As such, a quantitative risk assessment for chronic exposure was not carried out. For non-target organisms where the level of concern (LOC) is exceeded (i.e. RQ $\geq$1), a refined tier 1 assessment was conducted to determine the time required for concentrations to drop to levels low enough for the level of concern to no longer be exceeded. (i.e. RQ < 1.) For the screening level risk assessment, risk quotients for hydrogen peroxide were calculated based on the highest maximum net pen and wellboat target dose concentration of 1800 mg/L. The calculated screening level risk quotients for hydrogen peroxide are summarized in Appendix I, Table 4. For the refined tier 1 assessment, EECs as a function of time post release and distance from a net pen or wellboat were used. These EECs were derived from field dissipation monitoring studies and are presented in Appendix I, Tables 5 and 8. For net pens, the calculated EECs represent the concentration of hydrogen peroxide within the plume at a reported given point in time. For wellboats, the calculated EECs represent the concentration of hydrogen peroxide within the plume at a distance of 10 metres from the wellboat flushing pipe at a reported given point in time. The 10 metre distance from the wellboat flushing pipe was chosen as any non-target organisms found directly adjacent to the wellboat flushing pipe would be pushed by the velocity of the jets to the 10 metre distance in less than 1 minute. Ten (10) metre also represents an appropriate distance for the evaluation of exposure of non-target benthic organisms from wellboats with vertical downward discharge jets. As the concentration of hydrogen peroxide in the water dissipates over time, the risk quotients for non-target organisms are reduced. The time required before the risk quotients fall below the level of concern is presented in Appendix I, Tables 6 and 7 for net pens and Appendix I, Table 9 for wellboats. Where a 1-hour endpoint was available, the refined risk assessment focused on the 1-hour endpoint as Appendix I, Tables 6, 7 and 9 illustrate that for most organisms, the 1 hour exposure duration better approximates the anticipated time in which a non-target organism would be exposed to concentrations of hydrogen peroxide high enough to result in risk quotients that exceed the level of concern.

Invertebrates

Scallops and mussels

Hydrogen peroxide was practically non-toxic to scallops and mussels. The 48 hour LC_{50} for both species was reported to be greater than 3500 mg/L. The risk quotients for scallops and mussels resulting from exposure to hydrogen peroxide did not exceed the level of concern at the screening level. The use of hydrogen peroxide is expected to pose a negligible risk to scallops or mussels.

Green crabs and *Gammarus*

Hydrogen peroxide was practically non-toxic to green crabs and *Gammarus*. The 48 hour LC_{50} for both green crabs and *Gammarus* was reported to be greater than 350 mg/L. The risk quotients for green crabs and *Gammarus* did exceed the level of concern at the screening level. The refined assessment indicates that hydrogen peroxide could pose a risk to green crabs and *Gammarus* for approximately 0.18 hours post release, at a maximum distance of approximately 0.2 kilometres from the aquaculture net pen and a patch area of approximately 0.002 square kilometres. In situations where two net pens are treated simultaneously and the plumes overlap with one another, hydrogen peroxide is expected to pose a risk to green crabs and *Gammarus* for approximately 0.32 hours post release, at a distance up to 0.2 kilometres from the aquaculture net pen and over a patch area of less than 0.004 square kilometre total area. Hydrogen peroxide would also be anticipated to pose a risk to green crabs and *Gammarus* for approximately 1 minute, at a distance of 10 metres from a wellboat flushing jet and a patch area of approximately 0.0004 square kilometres. However, the toxicity endpoints were generated over an exposure period of 48 hours which is significantly longer than the anticipated exposure period under normal use conditions and therefore may overestimate risk. Furthermore, the calculated screening level risk quotients are lower than what is being reported due to the LC_{50} endpoint being greater than 350 mg/L. As such the use of hydrogen peroxide is expected to pose a negligible risk to green crabs or *Gammarus*.

Adult Lobster

Hydrogen peroxide was practically non-toxic to adult lobster. The 48 hour LC_{50} for adult lobster was reported to be 1390 mg/L. The 1 hour LC_{50} for adult lobster was reported to be 3750 mg/L. The risk quotients for adult lobster resulting from exposure to hydrogen peroxide did not exceed the level of concern at the screening level. The use of hydrogen peroxide is expected to pose a negligible risk to adult lobster.

Stage 1 Lobster larvae

A 48 hour LC_{50} for stage 1 lobster larvae was not available. However, the 1 hour LC_{50} for stage 1 lobster larvae was reported to be 1637 mg/L. The risk quotients for stage 1 lobster larvae did exceed the level of concern at the screening level and a refined assessment was conducted. The refined assessment indicates that the level of concern would no longer be exceeded in less than 1 minute post release from a net pen or wellboat. In situations where two net pens are treated simultaneously and the plumes overlap with one another, hydrogen peroxide is expected to pose a risk to stage 1 lobster larvae for less than 1 minute post release. As the times before the risk quotient drops below the level of concern are so short (less than 1 minute), hydrogen peroxide is expected to pose a negligible risk to stage 1 lobster larvae.

Crangon

A 48 hour LC_{50} for crangon was not available. However, the 1 hour LC_{50} for crangon was reported to be 3182 mg/L. The risk quotients for crangon did exceed the level of concern at the screening level and a refined assessment was conducted. The refined assessment indicated that the level of concern would no longer be exceeded less than 1 minute post release from a net pen and wellboat. In situations where two net pens are treated simultaneously and the plumes overlap with one another, hydrogen peroxide is expected to pose a risk to crangon for less than 1 minute post release. As the times before the risk quotient drops below the level of concern are so short (less than 1 minute), hydrogen peroxide is expected to pose a negligible risk to crangon.

Mysid

A 48 hour LC_{50} for mysid was not available. However, the 1 hour LC_{50} for mysid was reported to be 973 mg/L. The risk quotients for mysid did exceed the level of concern at the screening level and therefore a refined assessment was conducted. The refined assessment indicated that the level of concern would no longer be exceeded in less than 2 minutes post release from a net pen and less than 1 minute post release from a wellboat. In situations where two net pens are treated simultaneously and the plumes overlap with one another, hydrogen peroxide is expected to pose a risk to mysid for less than 2 minutes post release. As the times before the risk quotient drops below the level of concern are so short (less than 2 minutes), hydrogen peroxide is expected to pose a negligible risk to mysid.

Marine fish

A quantitative risk assessment was not conducted for marine fish. However, the target host for the end-use product is Atlantic salmon and efficacy studies have not reported high rates of Atlantic salmon mortality when the product is used according to the label directions. Given the rapid field dissipation of hydrogen peroxide coupled with low observations of fish mortality to the Atlantic salmon host crop, hydrogen peroxide is expected to pose a negligible risk to non-target fish.

Marine mammals

A quantitative risk assessment was not conducted for marine mammals. However, due to the very fast field dissipation rates and the very low potential for bio-accumulation and biomagnification, hydrogen peroxide is expected to pose a negligible risk to marine mammals.

Birds

A quantitative risk assessment was not conducted for birds. However, due to the very fast field dissipation rates and the very low potential for bio-accumulation and biomagnification, hydrogen peroxide is expected to pose a negligible risk to birds.

Marine algae

Hydrogen peroxide is highly toxic to marine algae. The EC_{50} (duration not reported) for the marine algae *Nitzchia closterium was* reported as 0.85 mg/L. The risk quotients for marine algae did exceed the level of concern at the screening level and therefore a refined assessment was conducted. The refined assessment indicated that hydrogen peroxide would pose a risk to marine algae for approximately 5.6 hours post release from a net pen, at a distance greater than 2 kilometres from the aquaculture net pen and a patch area of approximately 0.42 square kilometres. In the case of two net pens being treated simultaneously, hydrogen peroxide is expected to pose a risk to marine algae for approximately 7.4 hours post release where the plumes overlap, at a distance greater than 2 kilometres from the aquaculture net pen and over a patch area of approximately 0.84 square kilometres total area for both net pen treatments. Hydrogen Peroxide is expected to pose a risk to marine algae for approximately 46 minutes post release from a wellboat, at a maximum distance of 0.38 kilometres from the wellboat flushing jet and a patch area of approximately 0.029 square kilometres. However, due to the rapid reproduction rates of algae species coupled with the introduction of new ocean waters through the tidal flushing, any negative impacts to algal communities are expected to be transient.

5.0 Value

5.1 Effectiveness Against Pests

A total of 8 studies were reviewed in support of the control claims for Interox Paramove 50. These studies included several foreign trials, one study and one performance report on commercial treatments conducted in New Brunswick, and an expert report prepared by the Institute of Aquaculture laboratory at the University of Sterling, UK.

The target application rate tested by most studies was 1500 ppm. Rates lower than 1500 ppm were less effective, while higher rates were only marginally more effective. An application rate range of 1200 to 1800 ppm was supported by the reviewed information. At higher water temperatures Atlantic salmon are more susceptible to injury from H_2O_2; therefore, lower rates are required at higher water temperatures to ensure the fish are not injured. Atlantic salmon are more tolerant of H_2O_2 applications at lower temperatures, therefore, rates up to 1800 ppm may be used and have value as the concentration of H_2O_2 rapidly decreases in the water after application. While most submitted information was on *Lepeiophtheirus* spp., some information was submitted on *Caligus* spp. Extrapolation from the submitted data on *Lepeiophtheirus* spp. to *Caligus* spp. is possible because of similarity in biology of the two pests and the method by which H_2O_2 dislodges sea lice. Therefore, both genera of sea lice are supported based on the submitted information.

The reviewed studies demonstrated that Interox Paramove 50 is not as effective against juvenile attached life stages compared to motile pre-adult and adult life stages. In addition, it was demonstrated that that sea lice may recover and are capable of re-attaching to hosts following treatment, and that some treated egg strings will remain viable and hatch. As a result, there is a risk of re-infection by dislodged sea lice following treatment, which would require subsequent

re-treatment. To mitigate the risk of re-infestation labels statements including a warning that Interox Paramove 50 is not effective against all life stages and recommendations that steps should be taken to remove lice floating on the water after treatment in pens and to screen out sea lice in discharge water when using a wellboats are required.

5.2 Consideration of Benefits

5.2.1 Social and Economic Impact

Sea lice are a highly detrimental pest to farmed Atlantic salmon, heavy infestations can result in effects ranging from high mortality up to complete loss of infested fish. There are few alternatives available for treatment of this pest. Therefore, the registration of Interox Paramove 50 will provide a benefit to aquaculturists.

5.2.2 Survey of Alternatives

There are a limited number of products currently available to control sea lice. These products are two veterinary drugs, Slice (ememectin benzoate) and Calicide (teflubenzuron), and one pesticide, Salmosan 50 WP (azamethiphos, Registration Number 29466, available under an emergency use registration which expires 3 June 2014) (Appendix I, Table 10). These products also have limitations, such as the resistance of sea lice to Slice, and the fact that other products only target specific sea lice life stages. The registration of Interox Paramove 50 will provide an additional control product for use against this serious pest.

5.2.3 Compatibility with Current Management Practices Including Integrated Pest Management

Interox Paramove 50 is compatible with current pest management practices for farmed Atlantic salmon. The methods used to apply this product (tarped sea cages, wellboats) have already been adapted by Canadian Atlantic salmon aquaculturists for treatment of sea lice.

5.2.4 Information on the Occurrence or Possible Occurrence of the Development of Resistance

While there have been reports that sea lice have developed resistance to hydrogen peroxide treatments in certain regions of Europe, the mechanism of this is not known as the mode of action of hydrogen peroxide on sea lice has not been determined. It is suspected that re-attachment and re-infection by surviving sea lice following treatment may select for sea lice which are more tolerant to hydrogen peroxide treatments. The risk of re-infestation by dislodged sea lice can be mitigated using various methods to physically capture the dislodged sea lice.

5.3 Supported Uses

From a value perspective, application of Interox Paramove 50 for treatment of Atlantic salmon infested with sea lice at an application rate of 1200 to 1800 ppm (depending on temperature) for 20 to 30 minutes as a bath treatment using wellboats or fully tarpaulined net pens to remove sea lice from infested Atlantic salmon is supported (Appendix I, Table 11).

6.0 Pest Control Product Policy Considerations

6.1 Toxic Substances Management Policy Considerations

The Toxic Substances Management Policy (TSMP) is a federal government policy developed to provide direction on the management of substances of concern that are released into the environment. The TSMP calls for the virtual elimination of Track 1 substances [those that meet all four criteria outlined in the policy, i.e. persistent (in air, soil, water and/or sediment), bio-accumulative, primarily a result of human activity and toxic as defined by the *Canadian Environmental Protection Act*].

Interox M-70 Hydrogen Peroxide (including its transformation products), Interox CPMC-50, and Interox Paramove 50 were assessed in accordance with the PMRA Regulatory Directive DIR99-03[5] and evaluated against Track I criteria. The PMRA reached the following conclusions:

- Hydrogen Peroxide does not meet the Track 1 criteria and is not considered a Track 1 substance, as the active ingredient is not highly toxic, and is not expected to be persistent in the environment or to bioaccumulate. See Appendix I, Table 12 for comparison with Track 1 criteria.

- There are also no formulants, contaminants or impurities present in the end-use product Interox Paramove 50 that would meet the TSMP Track 1 criteria.

- Hydrogen Peroxide is not expected to form any transformation products that meet all Track 1 criteria.

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5 Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*

6.2 Formulants and Contaminants of Health or Environmental Concern

During the review process, contaminants in the technical and formulants and contaminants in the end-use product are compared against the *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* maintained in the *Canada Gazette*.[6] The list is used as described in the PMRA Notice of Intent NOI2005-01[7] and is based on existing policies and regulations including: DIR99-03; and DIR2006-02[8] and taking into consideration the Ozone-depleting Substance Regulations, 1998, of the *Canadian Environmental Protection Act* (substances designated under the Montreal Protocol). The PMRA has reached the following conclusions:

- Technical grade hydrogen peroxide, Interox M-70 Hydrogen Peroxide, Interox CPMC-50, and Interox Paramove 50 do not contain any formulants or contaminants of health or environmental concern identified in the *Canada Gazette*.

- The use of formulants in registered pest control products identified in the *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* maintained in the *Canada Gazette*[9] is assessed on an ongoing basis through PMRA formulant initiatives and Regulatory Directive DIR2006-02.

7.0 Summary

7.1 Human Health and Safety

The available information for the active ingredient hydrogen peroxide acid is adequate to qualitatively identify the toxicological hazards that may result from human exposure to the end-use product, Interox Paramove 50. Hydrogen peroxide is considered to be corrosive to skin, eyes and mucous membranes, with its oral, dermal and inhalation toxicities being secondary to corrosivity.

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6 *Canada Gazette*, Part II, Volume 139, Number 24, SI/2005-11-30) pages 2641-2643: *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* and in the order amending this list in the *Canada Gazette*, Part II, Volume 142, Number 13, SI/2008-67 (2008-06-25) pages 1611-1613: *Part 1 Formulants of Health or Environmental Concern, Part 2 Formulants of Health or Environmental Concern that are Allergens Known to Cause Anaphylactic-Type Reactions and Part 3 Contaminants of Health or Environmental Concern.*

7 Notice of Intent NOI2005-01, *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern under the New Pest Control Products Act*

8 Regulatory Directive DIR2006-02, *Formulants Policy and Implementation Guidance Document.*

9 *Canada Gazette*, Part II, Volume 139, Number 24, SI/2005-114 (2005-11-30) pages 2641–2643: *List of Pest Control Product Formulants and Contaminants of Health or Environmental Concern* and in the order amending this list in the *Canada Gazette*, Part II, Volume 142, Number 13, SI/2008-67 (2008-06-25) pages 1611-1613. *Part 1 Formulants of Health or Environmental Concern, Part 2 Formulants of Health or Environmental Concern that are Allergens Known to Cause Anaphylactic-Type Reactions and Part 3 Contaminants of Health or Environmental Concern.*

Workers involved in mixing, loading, and applying Interox Paramove 50, and clean-ups, repairs, and other activities immediately after application are not expected to be exposed to levels of hydrogen peroxide that will result in an unacceptable risk when Interox Paramove 50 is used according to label directions. The personal protective equipment on the product label is adequate to protect workers potential dermal, inhalation, and ocular exposures to hydrogen peroxide. Bystander exposure is expected to be negligible.

Dietary exposure to hydrogen peroxide from the use of the proposed end-use product is not expected to result in unacceptable dietary risks when the product is used according to label directions. The Agency did not establish a maximum residue limit (MRL) for hydrogen peroxide.

7.2 Environmental Risk

Hydrogen Peroxide is expected to pose a short term risk to marine algae. However, due to the rapid reproduction rates of algae species coupled with the introduction of new ocean waters through the tidal flushing, hydrogen peroxide is not expected to pose a risk to algae populations. Hydrogen Peroxide is not expected to pose a risk to any other non-target marine organisms such as mammals, crustaceans, birds, or fish.

7.3 Value

Interox Paramove 50 has value for use against sea lice as when it is used at an application rate of 1200 to 1800 ppm (depending on temperature) for 20 to 30 minutes as a bath treatment using wellboats or fully tarpaulined net pens. It is effective at removing pre-adult and adult life stages from infested Atlantic salmon. Sea lice are a highly detrimental pest to farmed Atlantic salmon: heavy infestations can result in effects ranging from high mortality up to complete loss of infested fish. Interox Paramove 50 is not as effective against juvenile attached life stages compared to motile pre-adult and adult life stages. In addition, some sea lice may recover and re-attach to hosts, and some treated egg strings may viable and hatch following treatment. While this results in a risk of re-infestation by dislodged sea lice, it can be mitigated using various methods to physically capture the dislodged sea lice.

8.0 Proposed Regulatory Decision

Health Canada's PMRA, under the authority of the *Pest Control Products Act* and Regulations, is proposing full registration for the sale and use of Interox M-70 Hydrogen Peroxide, Interox CPMC-50 and Interox Paramove 50, containing the technical grade active ingredient hydrogen peroxide, for the treatment of sea lice on Atlantic salmon reared in marine aquaculture sites.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

List of Abbreviations

λ	wavelength
ACGIH	American Conference of Governmental Industrial Hygienists
a.i.	active ingredient
BAF	Bioaccumulation Factor
BCF	Bioconcentration Factor
bw	body weight
CAS	Chemical Abstracts Service
CEPA	*Canadian Environmental Protection Act*
cm	centimetres
DACO	Data Code
DNA	deoxyribonucleic acid
DT_{50}	dissipation time 50% (the dose required to observe a 50% decline in concentration)
DT_{90}	dissipation time 90% (the dose required to observe a 90% decline in concentration)
EC_{50}	effective concentration on 50% of the population
ECETOC	European Centre for Ecotoxicology and Toxicology of Chemicals
EEC	estimated environmental exposure concentration
g	gram
H_2O_2	hydrogen peroxide
h	hour(s)
IBC	intermediate bulk container
ISO	International Organization for Standardization
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram
K_{oc}	organic-carbon partition coefficient
K_{ow}	*n*–octanol-water partition coefficient
L	litre
LC_{50}	lethal concentration 50%
LD_{50}	lethal dose 50%
LOC	level of concern
m	metre(s)
mg	milligram
MRL	maximum residue limit
N/A	not applicable
NIOSH	National Institute for Occupational Safety and Health
nm	nanometre(s)
Pa	pascals
PCPA	*Pest Control Products Act*
pH	potential of hydrogen
p*K*a	dissociation constant
PMRA	Pest Management Regulatory Agency
PPE	Personal protective equipment
ppm	parts per million

PVC	polyvinyl chloride
RA	risk assessment
RED	Reregistration Eligibility Decision document
RQ	risk quotient
SN	solution
TSMP	Toxic Substances Management Policy
TWA-TLV	Time weighted average-Threshold limit value
UK	United Kingdom
USEPA	United States Environmental Protection Agency
UV	ultraviolet

Appendix I Tables and Figures

Table 1 Summary of acute toxicity, irritation and sensitization information for hydrogen peroxide

STUDY	SPECIES/STRAIN AND DOSES	RESULT	TARGET ORGAN / SIGNIFICANT EFFECTS / COMMENTS	REFERENCE (PMRA No.)
Oral toxicity	Rat PRDD2000-02 ECETOC, 1993	LD_{50} (♀) = 1193 mg/kg bw (35%) LD_{50} (♂) = 1270 mg/kg bw (35%) LD_{50} = 801 mg/kg (60 %) LD_{50} = 75 mg/kg (70 %) **Highly acutely toxic.**	Clinical signs included tremors. Decreased motility, prostration and oral, ocular and nasal discharge.	1845944
Dermal	Rabbit ECETOC, 1993	LD_{50} (rabbit; 35%) = 2000 mg/kg bw LD_{50} (rabbit; 70%) = 6500 mg/kg **Slightly acutely toxic.**	Clinical signs included lacrimation and nasal discharge.	1845945
Inhalation	Rat ECETOC, 1993	LC_{50} (rat; 50%) > 0.17 mg/L LC_{50} (rat; 90%) > 0.338 – 0.427 mg/L **Moderately acutely toxic.**	Clinical signs included severe pulmonary congestion emphysema, decreased activity, eye closure, red nasal discharge.	1845947
Eye Irritation Draize method	Rabbit PRDD2000-02	**Corrosive.**	Not specified.	1845948
Dermal Irritation Draize method	Rabbit USEPA RED	**Corrosive.**	Not specified.	1845949
Dermal Sensitization Buehler test	Guinea pig ECETOC, 1993	Negative results. Not a dermal sensitizer.	Not specified.	1845950

Table 2 Fate and Behaviour in the Aquatic Environment

Study type	Value	Transformation products	Comments
Abiotic transformation			
Abiotic redox reactions In seawater	DT_{50} = 2.5 days	O_2 & H_2O	Non-Persistent
Phototransformation in water	DT_{50} = 10 days	O_2 & H_2O	Non-Persistent
Biotransformation			
Biotransformation in aerobic water systems	< 0.04 – 10 days	O_2 & H_2O	Non-Persistent
Biotransformation in anaerobic water systems	N/A	O_2 & H_2O	
Partitioning			
Adsorption / desorption in sediment	K_{oc} = 0.831	N/A	Does not bind.
Field studies			
Field dissipation	DT_{50} = 1 minute	O_2 & H_2O	Non-Persistent
Field dissipation	DT_{90} = 10 minutes	O_2 & H_2O	Non-Persistent

Table 3 Toxicity to Non-Target Species

Marine species	Exposure	Endpoint value (mg/L)	Degree of toxicity[b]
Green crabs	48-h EC_{50}	> 350	Practically non-toxic
Gammarus sp.	48-h LC_{50}	> 350	Practically non-toxic
Scallops	48-h LC_{50}	> 3500	Practically non-toxic
Mussels	48-h LC_{50}	> 3500	Practically non-toxic
Lobster	48-h LC_{50}	1390	Practically non-toxic
Mysid	48-h LC_{50}	< 35	Not determined
Lobster Larvae Stage 1	1-h LC_{50}	1637	Practically non-toxic
Lobster Adult	1-h LC_{50}	> 3750	Practically non-toxic
Mysid	1-h LC_{50}	973	Practically non-toxic
Crangon	1-h LC_{50}	3182	Practically non-toxic
Freshwater Algae *(Chlorella vulgaris)*[a]	72-h EC_{50}	2.5	Moderately Toxic
Marine Algae *(Nitzchia closterium)*	EC_{50} (duration not reported)	0.85 mg/L	Highly Toxic

[a] Used as a surrogate for marine species.
[b] Atkins *et al.*(1981) for bees and USEPA classification for others, where applicable

Table 4 Screening level risk assessment to aquatic organisms from hydrogen peroxide inside a net pen during or within the well of a wellboat during treatment

Organism	Exposure	Endpoint value (mg/L)	Uncertainty factor	Endpoint value for RA	Net pen / Wellboat target dose concentration (mg/L)	RQ	LOC exceeded
Marine species							
Green crabs	48-h EC_{50}	> 350	2	> 175	1800	< 10	Yes
Gammarus sp.	48-h EC_{50}	> 350	2	> 175	1800	< 10	Yes
Scallops	48-h EC_{50}	> 3500	2	> 1750	1800	< 1	No
Mussels	48-h EC_{50}	> 3500	2	> 1750	1800	< 1	No
Lobster	48-h EC_{50}	< 3500 > 350	2	> 175	1800	< 10	Yes
Mysid	48-h EC_{50}	< 35	2	< 18	1800	> 100	Yes
Lobster Larvae Stage 1	1-h LC_{50}	1637	2	818	1800	2.2	Yes
Lobster Adult	1-h LC_{50}	3750	2	1875	1800	0.96	No
Mysid	1-h LC_{50}	973	2	486	1800	3.7	Yes
Crangon	1-h LC_{50}	3182	2	1591	1800	1.1	Yes
Freshwater Algae *(Chlorella vulgaris)*[a]	72-h EC_{50}	2.5	2	1.25	1800	1440	Yes
Marine Algae (*Nitzchia closterium*)	Acute EC_{50} Duration Not reported	0.85	2	0.425	1800	4235	Yes

[a] Used as a surrogate for marine species.

Table 5 Estimated environmental concentrations (mg a.i./L) of hydrogen peroxide in the treatment plume after release from a 100 metre perimeter fish pen.

Time after release (hours)	Pelagic water column EECs within a plume post release from 100 (m) net pen circumference	Average area occupied by the plume (m^2)	Distance travelled by the plume (m)
	1800 mg/L treatment		
0	1800.00	800	0
0.1	270	1000	60
1	14	70000	400
2	4	140000	1800
3	2	220000	> 2000
4	1	300000	> 2000
5	0.54	370000	> 2000
6	0.43	450000	> 2000
7	0.24	530000	> 2000
7.5	0.20	560000	> 2000

Table 6 Estimated time required before the risk quotients fall below the level of concern after hydrogen peroxide is released from a 100 metre perimeter net pen.

Organism	Exposure	Endpoint value (mg/L)	Uncertainty factor	Endpoint value for RA	Time (hours)
Marine species					
Green crabs	48-h EC_{50}	> 350	2	> 175	< 0.18
Gammarus sp.	48-h EC_{50}	> 350	2	> 175	< 0.18
Lobster Larvae Stage 1	1-h LC_{50}	1637	2	818	< 0.01
Mysid shrimp	1-h LC_{50}	973	2	486	0.03
Crangon	1-h LC_{50}	3182	2	1591	< 0.01
Freshwater Algae *(Chlorella vulgaris)*[a]	72-h EC_{50}	2.5	2	1.25	3.5
Marine Algae (*Nitzchia closterium)*	Acute Duration Not reported	0.85	2	0.425	5.6

[a] Used as a surrogate for marine species.

Table 7 Estimated time required before the risk quotients fall below the level of concern after hydrogen peroxide is released from two adjacent 100 metre perimeter net pens.

Organism	Exposure	Endpoint value (mg/L)	Uncertainty factor	Endpoint value for RA	Time (hours)
Marine species					
Green crabs	48-h EC_{50}	> 350	2	> 175	< 0.32
Gammarus sp.	48-h EC_{50}	> 350	2	> 175	< 0.32
Lobster Larvae Stage 1	1-h LC_{50}	1637	2	818	N/A[b]
Mysid shrimp	1-h LC_{50}	973	2	486	N/A[b]
Crangon	1-h LC_{50}	3182	2	1591	N/A[b]
Freshwater Algae *(Chlorella vulgaris)*[a]	72-h EC_{50}	2.5	2	1.25	4.7
Marine Algae (*Nitzchia closterium)*	Acute EC_{50} Duration Not reported	0.85	2	0.425	7.4

[a] Used as a surrogate for marine species.

[b] Not applicable as the risk quotients would drop below the level of concern before two plumes would come into contact with one another.

Table 8 Estimated environmental concentrations (mg a.i./L) of hydrogen peroxide as a function of time 10 metres away from the mouth of the wellboat jet.

Time after release (minutes)	EECs (mg/L)	Area occupied by the plume (m^2)	Distance travelled by the plume (m)
1	180	400	10
2	90	830	20
3	60	1250	30
4	45	1650	40
5	36	2100	50
10	24	4000	100
20	18	10000	200
30	2.2	16000	300
40	0.9	22000	330
50	0.2	29000	380

Table 9 Estimated time required before the risk quotients fall below the level of concern after hydrogen peroxide is released from a wellboat flushing jet.

Organism	Exposure	Endpoint value (mg/L)	Uncertainty factor	Endpoint value for RA	Time (minutes)
Marine species					
Green crabs	48-h EC_{50}	> 350	2	> 175	1
Gammarus sp.	48-h EC_{50}	> 350	2	> 175	1
Lobster Larvae Stage 1	1-h LC_{50}	1673	2	836	< 1
Mysid shrimp	1-h LC_{50}	973	2	486	< 1
Crangon	1-h LC_{50}	3182	2	1591	< 1
Freshwater Algae *(Chlorella vulgaris)*[a]	72-h EC_{50}	2.5	2	1.25	37
Marine Algae (*Nitzchia closterium)*	Acute Duration Not reported	0.85	2	0.425	46

[a] Used as a surrogate for marine species.

Table 10 Registered Alternatives (as of January 2014)

Crop	Pest	Registered Alternative			
		Active Ingredient	Product Name and Registration Number	Product Type[x]	Resistance Group No.
Farmed Atlantic salmon	Sea lice	Emamectin benzoate	Slice	Veterinary drug	6
		Teflubenzuron	Calicide	Veterinary drug	15
		Azamethiphos	Salmosan 50 WP (Registration Number 29466)	Conventional	1b

Table 11 List of Supported Uses

Proposed label claim	VSAD supported use claim
Removal of sea lice from infested farmed Atlantic salmon: apply at a rate of 1200 to 1800 ppm (depending on temperature) for 20 to 30 minutes as a bath treatment using wellboats or fully tarpaulined net pens.	Accepted as proposed.

Table 12 Toxic Substances Management Policy Considerations-Comparison to TSMP Track 1 Criteria

TSMP Track 1 Criteria	TSMP Track 1 Criterion value		Active Ingredient Endpoints	Transformation Products Endpoints
CEPA toxic or CEPA toxic equivalent[1]	Yes		Yes	-
Predominantly anthropogenic[2]	Yes		No	-
Persistence[3]:	Soil	Half-life ≥ 182 days	< 1 Day	-
	Water	Half-life ≥ 182 days	0.04-10 Days	-
	Sediment	Half-life ≥ 365 days	< 10 Days	-
	Air	Half-life ≥ 2 days or evidence of long range transport	Half-life and volatilisation are not important routes of dissipation and long-range atmospheric transport is unlikely to occur.	-
Bioaccumulation[4]	L_{og} K_{OW} ≥ 5		No	-
	BCF ≥ 5000		not available	-
	BAF ≥ 5000		not available	-
Is the chemical a TSMP Track 1 substance (all four criteria must be met)?			No, does not meet TSMP Track 1 criteria.	-

1 All pesticides will be considered CEPA-toxic or CEPA toxic equivalent for the purpose of initially assessing a pesticide against the TSMP criteria. Assessment of the CEPA toxicity criteria may be refined if required (i.e. all other TSMP criteria are met).

2 The policy considers a substance "predominantly anthropogenic" if, based on expert judgement, its concentration in the environment medium is largely due to human activity, rather than to natural sources or releases.

3 If the pesticide and/or the transformation product(s) meet one persistence criterion identified for one media (soil, water, sediment or air) than the criterion for persistence is considered to be met.

4 Field data (for example, BAFs) are preferred over laboratory data (for example, BCFs) which, in turn, are preferred over chemical properties (for example, L_{og} K_{OW}).

References

A. List of Studies/Information Submitted by Registrant

1.0 Chemistry

PMRA Document Number	References
1892484	Chemistry and Pharmacy Reports, DACO: 2.14 CBI
1892491	Chemistry and Pharmacy Reports, DACO: 2.14 CBI
1892495	Chemistry and Pharmacy Reports, DACO: 2.14 CBI
1892533	Chemistry and Pharmacy Reports, DACO: 2.14 CBI
1892534	Chemistry and Pharmacy Expert Report, DACO: 2.14 CBI
1892552	Chemistry and Pharmacy Reports, DACO: 2.14 CBI
2296414	2013, Product Chemistry, DACO: 2.1,2.2,2.3,2.3.1,2.4,2.5,2.6,2.7,2.8,2.9 CBI
2296415	Manufacturing Summary, DACO: 2.11.1 CBI
2296416	Description of Starting Materials, DACO: 2.11.2 CBI
2296417	Detailed Production Process Description, DACO: 2.11.3 CBI
2296418	Discussion of Formulation of Impurities, DACO: 2.11.4 CBI
2296419	Establishing Certified Limits, DACO: 2.12.1 CBI
2296420	2003, Hydrogen Peroxide for industrial use Determination of hydrogen peroxide content Titrimetric method, DACO: 2.13.1 CBI
2296422	Methodology/validation, DACO: 2.13.1 CBI
2296423	Confirmation of Identity, DACO: 2.13.2 CBI
2296424	Batch Data, DACO: 2.13.3 CBI
2296426	Impurities of Toxicological Concern, DACO: 2.13.4 CBI
2296427	Chemical and Physical Properties Waiver, DACO: 2.14 CBI
2332045	2013, Description of Starting Materials with MSDSs (version 2), DACO: 2.11.2 CBI
2332046	2013, Detailed Production Process Description (Version 2), DACO: 2.11.3 CBI
2332051	2013, Heavy Metals Waiver Request, DACO: 2.13.4 CBI
2296450	2013, Product Identification, DACO: 3.1.1,3.1.2,3.1.3,3.1.4 CBI
2296452	Starting materials, DACO: 3.2.1 CBI
2296453	Description of Formulation Process, DACO: 3.2.2 CBI
2296455	Discussion of Formation of Impurities of Toxicological Concern, DACO: 3.2.3 CBI
2296456	Establishing certified limits, DACO: 3.3.1 CBI
2296457	Enforcement Analytical Method, DACO: 3.4.1 CBI
2296458	2003, Hydrogen Peroxide for industrial use, Determination of hydrogen peroxide content, Titrimetric method, DACO: 3.4.1 CBI
2296459	Impurities of Toxicological Concern, DACO: 3.4.2 CBI
2296460	Chemical and Physical Properties Waiver, DACO: 3.5 CBI
2296462	Container Material and Description, DACO: 3.5.5 CBI
2332778	2013, Revised Description of Starting Material, DACO: 3.2.1 CBI
2332779	2013, Revised Description of the Formulating Process, DACO: 3.2.2 CBI
2296498	2013, Product Identification, DACO: 3.1.1,3.1.2,3.1.3,3.1.4 CBI

2296499 Starting materials, DACO: 3.2.1 CBI
2296500 Description of Formulation Process, DACO: 3.2.2 CBI
2296501 Discussion of Formation of Impurities of Toxicological Concern, DACO: 3.2.3 CBI
2296502 Establishing certified limits, DACO: 3.3.1 CBI
2296503 Enforcement Analytical Method, DACO: 3.4.1 CBI
2296504 2003, Hydrogen Peroxide for industrial use, Determination of hydrogen peroxide content, Titrimetric method, DACO: 3.4.1 CBI
2296505 Impurities of Toxicological Concern, DACO: 3.4.2 CBI
2296506 Chemical and Physical Properties Waiver, DACO: 3.5 CBI
2296507 Container Material and Description, DACO: 3.5.5 CBI
2326877 2013, Revised Description with amounts, DACO: 3.2.2 CBI
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2.0 Human and Animal Health

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2296511 2010, Environmental Sampling and Analytical Program for 50% Hydrogen Peroxide Application Using Full Tarp and Well Boat Containment, DACO: 8.2.3.6
2296517 2012, Paramove Degradation in Seawater, DACO: 8.2.3.6
2321390 2013, LOA for Solvay Chemicals Inc. from New Brunswick for the use of Interox Paramove 50 (Registration Number 29783), DACO: 0.8.6
2323771 2013, Clarification Response, DACO: 0.8
2323772 2013, PARAMOVE Analysis in Seawater by Manual Titration, DACO: 5.2

3.0 Value

2028408 2010, Conclusions from Interox Summary Statistics. Unpublished. Submitted with Sub. No. 2011-1251, DACO: 10.2
2028406 2010, Data summary table New Brunswick hydrogen peroxide commercial application efficacy data, Unpublished, Submitted with Sub. No. 2011-1251, DACO: 10.2
1892555 Toovey, J. and A. Lyndon, 2000. Effects of hydrogen peroxide, dichlorvos, and cypermethrin on subsequent fecundity of sea lice, *Lepeophtheirus salmonis*, under fish farm conditions. Bull. Eur. Ass. Fish Pathol. 20(6) 2000, 224-228, DACO: 10.2

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1892508 Johnson, S., J. Constible, and J. Richard 1993. Laboratory investigations on the efficacy of hydrogen peroxide against the salmon louse *Lepeophtheirus salmonis* and its toxicological and histopathological effects on Atlantic salmon *Salmo salar* and Chinook salmon *Oncorhynchus tshawytscha*. Diseases of Aquatic Organisms 17:197-204, DACO: 10.2

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B. Additional Information Considered

i) Published Information

1.0 Human and Animal Health

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2.0 Environment

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1.0 Environment

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